

1. A non-human animal, or a precursor thereof, comprising cells, a tissue, or an organ, or a precursor thereof, of another organism, but not the corresponding cells, tissue, or organ, or precursor thereof, that would otherwise naturally occur in the animal.
2. The non-human animal of claim 1, wherein the other organism is a human.
3. The non-human animal of claim 1, wherein the animal is selected from the group consisting of a cow, a sheep, a pig, a mouse, or a primate, such as a chimpanzee, monkey, or ape.
4. The non-human animal of claim 1, wherein the cells are selected from the group consisting of red blood cells, pancreatic islet cells, epithelial cells, neurons, and chondrocytes; the tissue is selected from the group consisting of blood, the retina, and cartilage; or the organ is selected from the group consisting of a pancreas, a heart, a liver, a kidney, intestine, a lung, or skin.
5. The non-human animal of claim 1, wherein the animal is generated by knocking out the function of a gene encoding GATA-2, LMO-2, a globin, the erythropoietin receptor, PDX-1, or Insulin Promoter Factor-1.


6. A method of generating an animal comprising cells, a tissue, or an organ of another organism, but not the corresponding cells, tissue, or organ that would otherwise naturally occur in the animal, the method comprising:
- a. Knocking out the function of a gene that is required for development of the cells, tissue, or organ in a cell of an animal to generate a genetically modified cloning cell;
 - b. Introducing nuclear genetic material of the cloning cell, or a derivative thereof, into a reprogramming cell from another organism, or fusing the cloning cell with the reprogramming cell;
 - c. Stimulating the resulting cell to develop into a blastocyst;
 - d. Introducing into the blastocyst donor embryonic stem cells of another organism; and
 - e. Implanting the resulting blastocyst into a pseudopregnant foster mother, where it develops into a chimeric animal that comprises cells, a tissue, or an organ that are derived from the donor embryonic stem cells, but not the corresponding cells, tissue, or organ that would otherwise naturally occur in the animal.

10009359-032902

7. A method of generating an animal comprising cells, a tissue, or an organ of another organism, but not the corresponding cells, tissue, or organ that would otherwise naturally occur in the animal, the method comprising:

- a. Knocking out the function of a gene that is required for development of the cells, tissue, or organ in a cell of an animal to generate a genetically modified cloning cell;
- b. Introducing nuclear genetic material of the cloning cell, or a derivative thereof, into a reprogramming cell, or fusing the cloning cell with the reprogramming cell;
- c. Stimulating the resulting cell to develop into an embryo;
- d. Implanting the embryo into a pseudopregnant foster mother; and
- e. Introducing donor stem cells of another organism into the developing embryo or fetus *in utero*, so that the resulting embryo or fetus develops into a chimeric animal that comprises cells, a tissue, or an organ derived from the donor stem cells, but not the corresponding cells, tissue, or organ that would otherwise naturally occur in the animal.

- 5 8. A method of generating an animal comprising cells, a tissue, or an organ of another organism, but not the corresponding cells, tissue, or organ that would otherwise naturally occur in the animal, the method comprising:
- 10 a. Knocking out the function of a gene that is required for development of the cells, tissue, or organ in a cell of an animal to generate a genetically modified cloning cell;
- b. Introducing nuclear genetic material of the cloning cell, or a derivative thereof, into a reprogramming cell, or fusing the cloning cell with the reprogramming cell;
- 15 c. Stimulating the resulting cell to develop into a morula;
- d. Disaggregating individual blastomeres of the morula;
- e. Constructing a chimeric morula by injecting the disaggregated blastomeres and disaggregated donor blastomeres of another organism into a zona pellucida or by aggregating the blastomeres of the two organisms; and
- 20 f. Implanting the reconstructed morula into a pseudopregnant foster mother, where it develops into a chimeric animal that produce cells, a tissue, or an organ derived from the donor blastomeres, but not the corresponding cells, tissue, or organ that would otherwise naturally develop in the animal.

- 25  9. The method of claim 6, 7, or 8, wherein the cloning cell is an embryonic, fetal, or adult fibroblast.
10. The method of claim 6, 7, or 8, wherein the reprogramming cell is an unfertilized enucleated egg from another organism of the same, or a different, species from which the cloning cell was obtained.
- 30 11. The method of claim 6, 7, or 8, wherein the function of the gene is knocked out by homologous recombination.

12. The method of claim 6, 7, or 8, wherein the nuclear genetic material of the cloning cell is introduced into the reprogramming cell by nuclear transfer.

5

13. The method of claim 6, wherein the donor cells are human embryonic stem cells.

14. The method of claim 7, wherein the donor cells are human stem cells.

10

15. The method of claim 8, wherein the donor blastomeres are human blastomeres.

15

- Sub A2 16.

A method of treating a patient in need of a transplant of a cell, tissue, or organ, comprising transplanting into the patient cells, a tissue, or an organ produced in the animal of claim 1 or by the method of claim 6, 7, or 8.

17. A cell, tissue, or organ produced by the method of claim 6, 7, or 8.

20

18. Use of a cell, tissue, or organ produced by the method of claim 6, 7, or 8 in the treatment of a patient in need of a transplant of a cell, tissue, or organ, by transplanting the cell, tissue, or organ into the patient.

25

19. Use of a cell, tissue, or organ produced by the method of claim 6, 7, or 8 in the preparation of a medicament for treatment of a patient in need of a transplant of the cell, tissue, or organ.

[illegible]